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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/896,791	06/29/2001	Anders Berkenstam	13425-040001 / 00244-US	8306

23911 7590 12/11/2002

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EXAMINER	
NICKOL, GARY B	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 12/11/2002

19

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/896,791	BERKENSTAM ET AL.	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11 and 13-21* is/are pending in the application.

4a) Of the above claim(s) *2,3,8-11,13-17 and 19-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-7 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. *09/896,791* .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *15* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The Election filed October 4, 2002 (Paper No. 16) in response to the Office Action of September 4, 2002 is acknowledged and has been entered.

Claims 1-11, 13-21 are pending.

Claims 2-3, 8-11, 13-17, and 19-21 have been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions.

Claims 1, 4-7, and 18 are currently under prosecution

Applicant's election with traverse of Group I, claims 1, 4-7, and 18 in Paper No 16 is acknowledged. The traversal is on the ground(s) that a search and examination of the inventions of Groups I and II would not impose a serious burden on the examiner because the claims of Groups I and II are directed to isolated nucleic acid molecules, isolated polypeptides encoded thereby, vectors comprising the nucleic acid sequence, and host cells harboring the vector. This is not found persuasive. MPEP 802.01 provides that restriction is proper between inventions which are independent or distinct. Here, the inventions of the various groups are distinct for the reasons set forth in Paper No. 14.

As to the question of burden of search, the inventions are classified differently, necessitating different searches in the literature. Further, classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not coextensive and is much more important in evaluating the burden of search. Different searches and issues are involved in the examination of each group.

For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Specification

The specification is objected to for the following reasons:

1. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.
2. The specification is objected to on page 1, line 5 for reciting, "The present invention relates a mammalian" which is grammatically incorrect.
3. The specification is also objected to on page 7, line 3 for reciting "complementary the" which is grammatically incorrect.
4. The specification is further objected to because it contains an embedded hyperlink and/or other form of browser-executable code (i.e. see page 14, line 1). Applicant is required to delete all embedded hyperlinks and/or other form of browser-executable codes. See MPEP § 608.01.

Claim Objections

Claim 1 is objected to in step b, line 2 for reciting "complementary the" which is grammatically incorrect.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4-7, and 18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth an isolated nucleic acid molecule comprising a nucleotide sequence set forth as SEQ ID NO:2 and therefore the written description is not commensurate in scope with the claims broadly drawn to also include nucleic acid molecules capable of hybridizing to complementary nucleic acid sequences and or degenerate nucleic acid molecules which code for biologically active mammalian IPAS polypeptides or functional equivalents thereof.

The claims are broadly drawn to an isolated nucleic acid molecule selected from:

(a) nucleic acid molecules comprising a nucleotide sequence set forth as SEQ ID NO:2;

(b) nucleic acid molecules comprising a nucleotide sequence capable of hybridizing, under stringent hybridization conditions, to a nucleotide sequence complementary to the polypeptide coding region of a nucleic acid molecule as defined in (a) and which codes for a biologically active mammalian IPAS polypeptide or a functionally equivalent modified form thereof; and

(c) nucleic acid molecules comprising a nucleic acid sequence which is degenerate as a result of the genetic code to a nucleotide sequence as defined in (a) or (b) and which codes for a

biologically active mammalian IPAS polypeptides or a functionally equivalent modified form thereof.

The claims further include vectors comprising said nucleic acid molecules, host cells harboring the vectors, and methods of producing an IPAS polypeptide comprising culturing the host cells.

The instant disclosure (see page 14, line 5) of a single species of a nucleic acid molecule (and encoded polypeptide) does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera. A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). Further, as written, the claims do not require that the nucleic acids possess any specific and or particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims broadly read on a genus of nucleic acids.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim(s) is structure in the form of a recitation of a wide variety of nucleic acid molecules. For example, the specification teaches (page 7, line 20+) that the invention encompasses nucleic acid

molecules beyond the sequence shown in SEQ ID NO:2, including nucleic acid molecules carrying modifications like substitutions, small deletions, insertions, or inversions. The specification further teaches that such nucleic acid molecules encompass degenerate variants of SEQ ID NO:2 (page 8, line 4+). However, there is no description of the conserved regions which are critical to the structure and function of the genus claimed. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the nucleic acid molecules encompassed and no identifying characteristic or property of the instant nucleic acid molecules is provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. With the exception of SEQ ID NOs:2, the skilled artisan cannot envision the detailed structure of the encompassed genus of nucleic acid molecules and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Also, adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of

ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly **variant**, the disclosure of a structure of one specific nucleic acid molecule is insufficient to describe the genus and full-length genes. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Therefore, only a isolated nucleic acid molecule comprising a nucleotide sequence set forth as SEQ ID NO:2, but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4-7, and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Gu *et al.* (Gene Expr. Vol. 7. No. 3, 1998, pages 205-213).

The claims are drawn to an isolated nucleic acid molecule selected from:

(a) nucleic acid molecules comprising a nucleotide sequence set forth as SEQ ID NO:2;

(b) nucleic acid molecules comprising a nucleotide sequence capable of hybridizing, under stringent hybridization conditions, to a nucleotide sequence complementary to the polypeptide coding region of a nucleic acid molecule as defined in (a) and which codes for a biologically active mammalian IPAS polypeptide or a functionally equivalent modified form thereof; and

(c) nucleic acid molecules comprising a nucleic acid sequence which is degenerate as a result of the genetic code to a nucleotide sequence as defined in (a) or (b) and which codes for a biologically active mammalian IPAS polypeptides or a functionally equivalent modified form thereof.

The claims are further drawn to a vector comprising the nucleic acid sequence as defined in Claim 1 (Claim 4); a replicable expression vector, which carries and is capable of mediating the expression of a nucleic acid sequence as defined in Claim 1 (Claim 5); a cultured host cell harboring a vector according to claim 4 (Claim 6); a method for production of a mammalian IPAS polypeptide, comprising culturing a host cell according to claim 6 under conditions whereby said polypeptide is produced, and recovering said polypeptide (Claim 7); and a cultured host cell harboring a vector according to Claim 5 (Claim 18).

Gu *et al.* teach a isolated nucleic acid molecule comprising a nucleotide sequence capable of hybridizing, under stringent hybridization conditions, to a nucleotide sequence complementary to the polypeptide coding region of a nucleic acid molecule as defined in (a) and which codes for a biologically active mammalian IPAS polypeptide or a functionally equivalent

modified form thereof. Gu *et al.* further teach nucleic acid molecules comprising a nucleic acid sequence which is degenerate as a result of the genetic code to a nucleotide sequence as defined in (a) or (b) and which codes for a biologically active mammalian IPAS polypeptides or a functionally equivalent modified form thereof (**see attached sequence comparison**). Gu *et al.* further teach cultured host cells comprising vectors for the purposes of producing and recovering the expressed polypeptide (page 207, 209, and Fig. 7). Further, although the reference does not specifically teach that the vector is a "replicable expression vector" according to Claim 5, the claimed vector appears to be the same as the prior art. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 703-305-7143. The examiner can normally be reached on M-F, 8:30-5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the

organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Gary B. Nickol, Ph.D.
Examiner
Art Unit 1642

GBN
December 9, 2002

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  JOURNAL   Submitted (04-SEP-2001) Cell and Molecular Biology, Karolinska
            Institutet, von Eulers Vagen 3, Stockholm S-171 77, Sweden
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  JOURNAL   Gene Expr. 7 (3), 205-213 (1998)
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  AUTHORS   Gu,Y.Z., Moran,S.M., Hogenesch,J.B., Wartman,L. and Bradfield,C.A.
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  JOURNAL   Submitted (16-APR-1998) Oncology, University of Wisconsin, 1400
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Db    441 ----------------------------------------------------CTGGAGCT 448

Qy    432 cattggacacagtatctttgattttatccatccctgtgaccaagaggaacttcaagacgc 491
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RESULT 3
RNO277827
LOCUS RNO277827 2077 bp mRNA linear ROD 26-FEB-2001
DEFINITION Rattus norvegicus mRNA for hypoxia inducible factor 3 alpha (Hif-3a gene).
ACCESSION AJ277827
VERSION AJ277827.1 GI:8953574
KEYWORDS Hif-3a gene; hypoxia inducible factor 3 alpha.
SOURCE Norway rat.
ORGANISM Rattus norvegicus
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.
REFERENCE 1 (bases 1 to 2077)
AUTHORS Kietzmann,T., Cornesse,Y., Brechtel,K., Modaressi,S. and Jungermann,K.
TITLE Perivenous expression of the mRNA of the three hypoxia-inducible factor alpha-subunits, HIF1alpha, HIF2alpha and HIF3alpha, in rat liver
JOURNAL Biochem. J. 354 (Pt 3), 531-537 (2001)
MEDLINE 21134367
REFERENCE 2 (bases 1 to 2077)
AUTHORS Kietzmann,T.
TITLE Direct Submission
JOURNAL Submitted (05-MAY-2000) Kietzmann T., Biochemistry I, Institut of Biochemistry and Molecular Cell Biology, Humboldtallee 23, D-37073 Goettingen, GERMANY
FEATURES Location/Qualifiers
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BASE COUNT 457 a 700 c 552 g 368 t
ORIGIN

Query Match 45.9%; Score 505.4; DB 10; Length 2077;
Best Local Similarity 84.3%; Pred. No. 2.5e-92;
Matches 623; Conservative 0; Mismatches 46; Indels 70; Gaps 2;

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Qy     26 tggggctgcagcgcgtgaggtcgaacaccgagctgcggaaggagaagtcgcgggacgcgg 85
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